

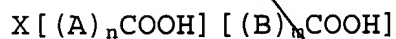
- (a) providing by solid phase synthesis or fragment coupling ligands comprising said peptide sequences, the ligands being attached to a solid phase,
- (b) deprotecting any protected N-terminal amino groups while the ligands are still attached to the solid phase,
- (c) reacting the ligands having unprotected N-terminal amino groups with an achiral di-, tri- or tetracarboxylic acid so as to provide a construct having a ring structure, and
- (d) cleaving the construct from the solid phase.

47. (New) A method according to claim 46 further comprising the steps of

- (c<sup>1</sup>) prior to step (d), deprotecting any N-protected amino groups originating from the carboxylic acid used in step (c),
- (c<sup>2</sup>) continuing the solid phase synthesis or fragment coupling so as to provide ligands comprising peptide sequences having at least one N-protected N-terminal amino group, and

(c<sup>3</sup>) deprotecting any protected N-terminal amino group(s) prior to step (d).

48. (New) The method according to claim 46, wherein the achiral acid used in step (c) is of the general formula



wherein n and m independently are an integer of from 1 to 20, X is HN, A and B independently are optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, an optionally substituted cyclic group, an optionally substituted heterocyclic group, or an optionally substituted aromatic group, or A and B together form an optionally substituted cyclic group, an optionally substituted heterocyclic group, or an optionally substituted aromatic group, or

n and m are 0 or an integer of from 1 to 20, X is H<sub>2</sub>N(CR<sub>2</sub>)<sub>p</sub>CR, or RHN(CR<sub>2</sub>)<sub>p</sub>CR, wherein p is 0 or an integer of from 1 to 20, wherein each R is H, optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, an optionally substituted cyclic group, an optionally substituted heterocyclic group, or an optionally substituted aromatic group, and A and B are both optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub>

alkenyl, an optionally substituted cyclic group, an optionally substituted heterocyclic group, or A and B together form an optionally substituted cyclic group, an optionally substituted heterocyclic group, or an optionally substituted aromatic group, or

*cont*

n and m are 0 or an integer of from 1 to 20, X is  $\text{HO}(\text{CR}_2)_p\text{CR}$ ,  $\text{HS}(\text{CR}_2)_p\text{CR}$ , halogen- $(\text{CR}_2)_p\text{CR}$ ,  $\text{HOOC}(\text{CR}_2)_p\text{CR}$ ,  $\text{ROOC}(\text{CR}_2)_p\text{CR}$ ,  $\text{HCO}(\text{CR}_2)_p\text{CR}$ ,  $\text{RCO}(\text{CR}_2)_p\text{CR}$ , or  $[\text{HOOC}(\text{A})_n][\text{HOOC}(\text{B})_m]\text{CR}(\text{CR}_2)_p\text{CR}$ , wherein p is 0 or an integer of from 1 to 20, each R independently is H, optionally substituted  $\text{C}_{1-10}$  alkyl, optionally substituted  $\text{C}_{2-10}$  alkenyl, an optionally substituted cyclic group, an optionally substituted heterocyclic group, or an optionally substituted aromatic group, and A and B are both optionally substituted  $\text{C}_{1-10}$  alkyl, optionally substituted  $\text{C}_{2-10}$  alkenyl, an optionally substituted cyclic group, an optionally substituted heterocyclic group, or A and B together form an optionally substituted cyclic group, an optionally substituted heterocyclic group, or an optionally substituted aromatic group, or

n and m are 0 or an integer of from 1 to 20, X is  $\text{H}_2\text{N}(\text{CR}_2)_p$ ,  $\text{RHN}(\text{CR}_2)_p$ ,  $\text{HO}(\text{CR}_2)_p$ ,  $\text{HS}(\text{CR}_2)_p$ , halogen- $(\text{CR}_2)_p$ ,  $\text{HOOC}(\text{CR}_2)_p$ ,  $\text{ROOC}(\text{CR}_2)_p$ ,  $\text{HCO}(\text{CR}_2)_p$ ,  $\text{RCO}(\text{CR}_2)_p$  or  $[\text{HOOC}(\text{A})_n][\text{HOOC}(\text{B})_m]$ , wherein p is 0 or an integer of from 1 to 20, each R independently is H,

optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, an optionally substituted cyclic group, an optionally substituted heterocyclic group, or an optionally substituted aromatic group, and A and B together form an optionally substituted cyclic group, an optionally substituted heterocyclic group, or an optionally substituted aromatic group.

49. (New) The method according to claim 46, wherein the achiral acid is a di- or tri-carboxylic acid.

CD/cont 50. (New) The method according to claim 46, wherein the achiral acid is selected among imino diacetic acid, 2-amino malonic acid, 3-amino glutaric acid, 3-methylamino glutaric acid, 3-chloro glutaric acid, 3-carboxymethyl glutaric acid, 3-methoxy-carbonyl glutaric acid, 3-acetyl glutaric acid, glutaric acid, tricarballic acid, 3,4-bis-carboxymethyl adipic acid, 4-(2-carboxyethyl)-pimelic acid, (3,5-bis-carboxymethylphenyl)-acetic acid, 3,4-bis-carboxymethyl-adipic acid, benzene-1,2,4,5-tetra carboxylic acid, 4-(3-carboxy-allylamino)-but-2-enoic acid, 4,4'-imino-dibenzoic acid, 1,4-dihydropyridine-3,5-dicarboxylic acid, 5-amino isophthalic acid, 2-chloro malonic acid, 3-hydroxy glutaric acid, and benzene-1,3,5-tricarboxylic acid.

selected-ASP

51. (New) The method according to claim 46, wherein the peptide sequences comprise naturally occurring amino acids or non-naturally occurring amino acids or a peptide nucleic acid (PNA) sequence.

52. (New) The method according to claim 47, wherein a chemical entity enhancing the solubility or immunogenicity of the LPA obtained, or being suitable for directing the LPA to its target, or being a marker, is attached to the N-terminal of the achiral carboxylic acid.

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53. (New) The method according to claim 52, wherein the chemical entity is selected from fatty acids, antibodies or peptides for directing the LPA to its target, fluorophores, biotin, enzymes such as horse radish peroxidase, alkaline phosphatase and soya bean peroxidase, or nucleic acid sequences.

54. (New) The method according to claim 46, wherein at least one of the peptide sequences comprises all or part of one or more B cell epitopes, all or part of one or more T cell epitopes, or all or part of one or more B and T cell epitopes, or mimics thereof.

55. (New) The method according to claim 54, wherein at least one of the peptide sequences is important for an immune response.

56. (New) ~~The method according to claim 46, wherein at least one of the peptide sequences is derived from OspC protein of *Borrelia burgdorferi*, or is a homologous sequence capable of reacting with anti-OspC antibodies or provoking an immune response.~~

57. (New) ~~The method according to claim 56, wherein the LPA obtained provide a C-terminal presentation of the C-terminal sequence Pro-Lys-Lys-Pro of OspC.~~

58. (New) ~~The method according to claim 46, wherein at least one of the peptide sequences is derived from the flagellum of *Borrelia burgdorferi* or is a homologous sequence capable of reacting with anti-flagellum antibodies.~~

59. (New) ~~The method according to claim 56, wherein the LPA obtained provide C-terminal presentation at least one peptide sequence derived from OspC of *Borrelia burgdorferi* and further comprises at least one peptide sequence derived from the flagellum of *Borrelia burgdorferi*.~~

60. (New) ~~The method according to claim 46, wherein at least one of the peptide sequences is derived from *Mycobacterium tuberculosis*.~~

61. (New) The method according to claim 56, wherein the LPA obtained further comprises at least one peptide sequence derived from *Mycobacterium tuberculosis*.

62. (New) The method according to claim 60, wherein at least one of the peptide sequences comprises the ESAT-6, 51-70 sequence protein or the ESAT-6, 1-17 sequence protein of *Mycobacterium tuberculosis*.

63. (New) The method according to claim 46, wherein the LPA obtained is selected from the group consisting of

[LPA-I]:  $\text{FmocN}(\text{CH}_2\text{CO-ProValValAlaGluSerProLysLysPro-OH})_2,$

[LPA-II]:  $\text{biotin-NH}(\text{CH}_2)_5\text{CON}(\text{CH}_2\text{CO-ProValValAlaGluSerProLysLysPro-OH})_2,$

[LPA-III]:  $\text{NH}_2\text{CH}(\text{CH}_2\text{CO-ProValValAlaGluSerProLysLysPro-OH})_2,$

[LPA-IV]:  $\text{H-Lys-NHCH}(\text{CH}_2\text{CO-ProValValAlaGluSerProLysLysPro-OH})_2,$

[LPA-VII]:  $\text{CH}_2(\text{CH}_2\text{CO-}\beta\text{-Ala-}\beta\text{-AlaLysGluProAsnLysGlyValAsnPro-AspGluVal}\beta\text{Ala})_2,$

[LPA-VIII]:  $\text{HC}(\text{CH}_2\text{CO-LysGluProAsnLysGlyValAsnProAspGluVal-}\beta\text{Ala})_2\text{COOH,}$

[LPA-IX]:  $\text{Fmoc-NHCH}(\text{CH}_2\text{CO-AspArgValTyrIleHisProPheHisLeu-NH}_2)_2,$

[LPA-X]:  $\text{Aloc-NHCH}(\text{CH}_2\text{CO-AspArgValTyrIleHisProPheHisLeu-NH}_2)_2$  and

[LPA-XI]:  $\text{Fmoc-AspProThrGlnAsnIleProProGly-NHCH}(\text{CH}_2\text{CO-AspArg-ValTyrIleHisProPheHisLeu-NH}_2)_2.$

64. (New) The method according to claim 56, wherein the LPA obtained further comprises at least one peptide sequence derived from the flagellum of *Borrelia burgdorferi* or a homologous sequence capable of reacting with anti-flagellum antibodies.

65. (New) The method according to claim 60, wherein the LPA obtained is selected from the group consisting of

[LPA-V]:  $(\text{HO-ProLysLysProSerGluAlaValValPro-COCH}_2)_2\text{CH-NH-Lys-(GlnLeuAlaAsnAsnLeuGluThrAlaThrAlaAspTrpLysGlnGlnValGlyGlnTyr-H)}_2,$  and



sub  
exp  
anal

[LPA-VI]: (HO-ProLysLysProSerGluAlaValValPro-COCH<sub>2</sub>)<sub>2</sub>N-Lys (AlaSer-  
AlaAlaAlaGluIleGlyAlaPheAsnTrpGlnGlnGluThrMet-H)<sub>2</sub>.

D/10  
anal

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